

SCIENCE, TECHNOLOGY AND INNOVATION ROUNDTABLE

Migraine Therapies in Women



- ▶ December 14, 2018
- ▶ MEETING REPORT

healthy
women

Overview

On December 14, 2018, HealthyWomen hosted a Science, Technology and Innovation Roundtable in Baltimore, MD to discuss Migraine Therapies in Women. Participants addressed women's experience with current migraine treatments and explored the availability and efficacy of noninvasive nondrug treatments. They reviewed barriers to the use of nondrug treatments from the perspective of both patients and health care providers and identified opportunities to overcome these barriers. The roundtable participants represented a variety of interests and experience related to migraine disease and included neurologists, nurse practitioners, a psychologist, a sleep specialist, and several women with migraine disease who shared insights into their migraine journeys. A list of participant names and affiliations is provided towards the end of this report.

Introduction

Migraine disease is a debilitating neurological disease that is three times more common in women than men. About 40% of women experience migraine disease by the end of their reproductive lifespan, with the highest susceptibility occurring during menarche, menstruation, postpartum and perimenopause.¹

The effects of migraine disease over a woman's lifespan can be devastating.² Headaches and other symptoms of migraine disease can become more frequent and severe over time, with some women experiencing nearly daily chronic headaches. Other women may delay having children or have fewer children because of migraine disease. Despite major medical breakthroughs, migraine disease remains among the top 10 human disabling disorders globally and is particularly burdensome in young and middle-aged women.³

Treating Migraine Disease in Women: A Life-Course Approach

Up to 70% of women with migraine report a menstrual or hormonal relationship with migraine attacks.¹ The times of highest susceptibility to migraine are associated with abrupt estrogen swings: menarche, menstruation, postpartum and perimenopause.^{1,4}

Current treatments for migraine disease vary across a woman's lifespan:

- ▶ **Menstrual cycle:** Evidence based mainstream treatment strategies for menstrual migraine typically involves using drugs such as Frovatriptan, Naratriptan or Naprosyn to prevent menstrual migraine. However, one strategy also involves eliminating ovulation and stabilizing estrogen levels with continuous use of combined oral contraceptives (COCs), the ethinyl estradiol (EE) ring, or the contraceptive patch. However, hormonal strategies may not be appropriate for all women and should be used with caution.⁵
- ▶ **Pregnancy:** Migraine with aura may worsen or present for the first time with higher estrogen levels during pregnancy. Triptans are considered Category C although a recent review found no increase in birth defects above the baseline for sumatriptan. Following delivery, the precipitous decline in estrogen combined with lack of sleep and stress may precipitate postpartum headaches, including migraine attacks. Women should plan ahead prior to conception to avoid triggers, reduce stress, discontinue medications that could potentially harm the fetus and improve sleep and nutrition.
- ▶ **Lactation:** Sumatriptan is considered compatible with breastfeeding by the American Academy of Pediatrics, but nursing mothers are frequently reluctant to use medications to treat or prevent migraine attacks. Prevention involves restorative sleep, which is difficult with a new infant.
- ▶ **Menopause:** Migraine prevalence increases during perimenopause and decreases after menopause for most women.¹ COC treatment may be used to lessen hormonal fluctuations during perimenopause. For some postmenopausal women, new guidelines recommend the use of estrogen support and transdermal products, especially if started during the early postmenopausal years (a critical window).

Many women are unable to use an effective preventive medication for migraine disease and are limited in their choices for contraception and treatment of other menstrual-related complaints. But, for women with migraine with aura, COCs are contraindicated due to the increased risk of ischemic stroke. However, this contraindication is based on data from the 1960s or 1970s when oral contraceptives contained high doses of estrogen.⁵

The participants agreed that OB/GYNs often treat migraine disease quite differently from headache specialists and neurologists, and that collaboration with OB/GYNs is important. For example, some OB/GYNs often start with hormonal strategies, and may underuse other strategies, while neurologists often start with drug strategies and rarely prescribe hormonal solutions.

Migraine disease remains underdiagnosed and undertreated. According to the Chronic Migraine Epidemiology and Outcomes (CaMEO) study, only 40.8% of patients currently consulted a health care professional for migraine disease. Of those, 10% were diagnosed accurately. Of those, 4.5% were prescribed appropriate treatment.⁶ The reasons for undertreatment of migraine disease include:

- 1) The most disabled patients may not be adequately informed by their practitioners about optimal management options.
- 2) There is no cure for migraine disease and current drug treatments for prevention are effective in no more than 30% to 50% of patients.
- 3) One out of four patients stop potentially effective drug treatments due to disabling side effects.

The participants agreed that while current drug therapies do provide relief for many patients, they also have many limitations. Drug therapies are limited by lack of efficacy, incomplete relief, recurrence, cost, coverage, quantity limits, adverse side effects, contraindications, pregnancy, inconvenience, and medication overuse. Discontinuation rates for acute and preventive migraine treatments are well over 50%.⁷

The participants also agreed that guidance is lacking for treating women with migraine disease. There are no randomized double-blind controlled clinical studies that provide agreement on hormonal management of migraine disease. The steps for starting COCs for migraine disease are not clear. More evidence-based data and consensus are also needed to determine the best treatments for women who have more complicated pain in addition to migraine disease.

In randomized controlled trials, the bar for efficacy is low, i.e., a 50% improvement in 50% of patients.⁸ Participants may not be specifically asked about other therapies that they are using, such as a hormone patch. Patients with certain comorbidities, such as cardiovascular conditions, major depression, bipolar disorder or other pain conditions are typically excluded from trials.⁷ Women should be informed that some commonly-used therapies have no data from large clinical trials.

Overview of Nondrug Options for Migraine Relief

Women who must discontinue or limit their migraine medications often feel that they are left without any options. Complementary and alternative medicine (CAM) is the most preferred nondrug treatment, where one out of two US adults with migraine disease or severe headaches uses CAM. Surprisingly, CAM is not on top of the minds of most prescribers—even neurologists and other specialists.⁹ Interestingly, of these, 50% do not discuss their nondrug treatments with their health care provider.¹⁰ Although nondrug treatments have shown no superiority over available drug treatments, they are well-tolerated overall and can be combined with conventional drug therapies. Some are effective for both preventive and acute treatment.

The most common nondrug practices used in the U.S. are meditation, breathing exercises, and yoga. Other complementary and integrative treatments include: natural products (e.g., riboflavin, magnesium, CoQ10, feverfew), behavioral therapies (e.g., cognitive behavioral therapy, acceptance-commitment therapy, biofeedback, exercise, hypnosis), manipulative and body-based practices (e.g., massage, chiropractic, acupuncture, cranio-sacral therapy), and devices—both invasive and noninvasive.

The participants agreed that behavioral therapy has been particularly helpful for women with migraine disease. Although it is not meant to be a medication substitute, therapy can be a good adjunct. Likely candidates for behavioral therapy are patients who experience one or more headaches per week or have significant disability, psychological comorbidities, acute medication overuse, significant life stress, or an interest in behavioral therapy.¹¹

The newest therapies for migraine disease are the noninvasive neuromodulation devices, which are placed on specific areas of the head or neck for short periods of time and work by modulating the actions of specific nerves involved in migraine pain. This new technology has shown promise in clinical trials and no significant side effects. Currently, three noninvasive devices have been cleared by the U.S. Food and Drug Administration (FDA) for both acute migraine and migraine prevention:

- ▶ **Cefaly:** placed on the forehead and turned on daily for 20 minutes; stimulates the supraorbital nerve. Cleared for acute and preventive migraine treatment.
- ▶ **gammaCore™:** placed on the neck and turned on to electrically stimulate the vagus nerve for 90 seconds to two minutes. Cleared for acute migraine treatment and in clinical trials for migraine prevention.
- ▶ **SpringTMS:** placed on the back of the head and turned on for a split-second pulse that provides transcranial magnetic stimulation. Cleared for acute and preventive migraine treatment with and without aura.

There are two other non-invasive devices that are being developed: Nerivio Migra, is a remote device to wear on the arm, and Neuroief, which goes around the forehead and mimics a neurostimulator but without the invasive surgery. Neither have been cleared by the FDA at the time of writing this paper.

The efficacy and safety of neurostimulation devices were evaluated in several clinical trials,¹²⁻¹⁹ which indicated that the FDA-cleared devices met the FDA standards for efficacy and safety. While not meant to be a substitute for medication, nondrug therapies can be useful when patients have little or incomplete relief with medications and another tool is needed. Patients that are likely to benefit from nondrug therapy include those who:

- ▶ Are extremely sensitive to conventional treatments
- ▶ Express a preference for nonconventional treatments
- ▶ Have exhausted conventional treatments in adequate trials
- ▶ Experience a significant role of stress or lifestyle in their triggers or disability
- ▶ Are unable to take conventional oral treatments due to drug interactions or other medical conditions
- ▶ Need migraine treatment during pregnancy

Barriers to the Use of Noninvasive Nondrug Treatments

At the Roundtable, two panels, representing the patient perspective and the health care provider perspective, discussed barriers to the use of noninvasive nondrug treatments and suggested options for overcoming the barriers.

PATIENT PERSPECTIVES

The panel of patients with migraine disease agreed that health care providers lack awareness of noninvasive therapies as treatment options for migraine disease. They cited a limited availability of in-network specialists, including neurologists, and a scarcity of certified headache specialists that would tend to have more knowledge about noninvasive medical devices.

Stigma is another major concern, with prejudice against women in particular. Women's symptoms are often passed off as stress, an inability to cope, a character flaw, a personality trait, or the lack of healthy lifestyle.

Another barrier is the lack of coverage of nondrug therapies by insurance companies, which require prior authorization and limit options through “fail first/step therapy” for medications, and generally deny coverage all-together for medical devices. The burden is on patients to gather and provide proof of medical necessity, and the appeals process is complicated.

Costs for nondrug therapies are high, going as high as \$575 per month for noninvasive medical devices. The costs for traditional drug therapies are often even higher, often going well over \$1,000 per month when considering doctor and medication copays, deductibles, and travel costs.

HEALTH CARE PROVIDER PERSPECTIVES

For clinicians, nondrug therapies are often not considered or offered. Gynecologists, primary care providers and many neurologists are not aware of devices. More education for practitioners is needed.

Noninvasive devices (gammaCore™, SpringTMS, and Cefaly) are poorly covered by insurance. The lack of coverage may be due to a lack of knowledge from insurance utilization managers. Insurance carriers use peer-reviewed clinical studies and guidelines from professional societies (such as those from the American Headache Society) to help them determine approval or denial of non-invasive/non-drug treatments. Devices are often considered either experimental, investigational or unproven. Although letters of appeal are an option, they are ineffective unless received in high enough numbers to force a change in the formulary.

Access and cost are often prohibitory, especially for patients without insurance. Even for patients with insurance, most plans have high deductibles. There is also a shortage of headache specialists, which particularly impacts patients with chronic headaches or high-frequency episodic migraine. There are often long wait times for appointments, sometimes extending over six months.

Pharmacological treatments remain first-line because nonpharmacological treatments are often not covered. The lack of coverage can result in a more chronic disease state, which then leads to higher overall costs.

SUGGESTIONS FOR OVERCOMING THE BARRIERS

The participants provided the following suggestions to help health care providers, employers, insurance companies, and the health care industry overcome barriers to the use of noninvasive nondrug treatments for migraine disease.

Patient Perspectives

HEALTH CARE PROVIDERS

- ▶ Provide patients with more education about noninvasive medical devices.
- ▶ Ensure that all acute/rescue treatments, including medical devices, are available in urgent care centers and emergency rooms.

EMPLOYERS

- ▶ Accommodate employees by, for example, improving lighting, having scent-free company policies, allowing flex-work time, and offering adequate health insurance plans.

INSURANCE COMPANIES

- ▶ Understand the long-term cost savings for covering noninvasive medical devices for prevention.
- ▶ Provide patients with clear easily understood information about insurance terms (e.g., co-pay vs. deductible) and appeal processes.
- ▶ Change Fail First/Step therapy policies and decisions to override doctors' prescriptions.

HEALTH CARE INDUSTRY

- ▶ Continue to support patient-centric advocacy organizations and headache disorders research.
- ▶ Improve the portrayal of migraine disease and other headache disorders in advertising
- ▶ Provide adequate medical education about headache disorders.
- ▶ Raise awareness about headache disorders across age, gender, economic and ethnic barriers.

ADVOCACY GROUPS

- ▶ Put pressure on insurance companies that deny access to treatment options.
- ▶ Raise awareness of the seriousness of migraine disease and openly address the stigma.

Health Care Provider Perspectives

HEALTH CARE PROVIDERS

- ▶ Educate insurance companies and patients.
- ▶ Include a wellness plan as part of the health care plan.
- ▶ Address psychological factors hindering care such as attitudes, beliefs, and motivation level and relevant comorbidities of anxiety, depression or insomnia.
- ▶ Plant the "seed" for preventative care, allowing more frequent regular office visits, increasing appointment times to teach patients about disease state and proper management.

EMPLOYERS

- ▶ Gain a better understanding of the migraine disease state, its epidemiology, its direct and indirect costs, and its effects on job performance and productivity.
- ▶ Understand when there is a need for accommodation, both preventively and abortively (e.g., no fluorescent lights, scent-free work environment, low noise levels).

INSURANCE COMPANIES

- ▶ Cover other modalities of treatment for headaches in general, i.e., nonpharmacological treatments such as medical devices, biofeedback and natural supplements.

HEALTH CARE INDUSTRY

- ▶ Continue to advocate for patients by marketing and by providing free samples, co-pay cards, and educational programs.

Patients' Personal Migraine Journeys

Four women with migraine disease shared their personal experiences with migraine disease and its treatments. Their migraine attacks had become more frequent and severe over time, with some experiencing nearly daily chronic headaches. After a while, they became intolerant to their medications, found them no longer effective, had intolerable side-effects, or experienced overuse headaches. Some were told "there is nothing more we can do."

The women said that practitioners, including neurologists, seemed limited in their knowledge about migraine disease. Getting an appropriate diagnosis was difficult. Physicians tended to attribute the symptoms to something else, like epilepsy, anxiety or cardiac conditions. The lack of communication among providers was not helpful.

Stigma was a major issue. The women encountered stigma in the medical profession, workplace, social environment, and even the migraine community. Viewing migraine disease as a character flaw or personality trait resulted in self-blame, which made it even more difficult to maneuver through disability and deal with the disease.

The women explored nondrug, nontraditional therapies on their own to help manage their pain. Frequently their physicians did not offer or even suggest these therapies. The women found it challenging to learn about these therapies and would have liked to have had support in their decisions. Some said they were afraid to tell their doctors about using nontraditional therapies because they wanted to avoid judgment.

Several women reported experiences with neurostimulator implants, which sometimes worked well for a while but eventually failed. Some had personal experience with the non-invasive medical devices, and they all felt that it was important to know that other options are available. One cited a friend who was able to stop her medications after using a noninvasive medical device from Canada.

All of the women said that they found it meaningful to share their experiences through advocacy groups, which they either joined or founded on their own. Discovering that they were not alone was very empowering.

Key Takeaways and Recommendations

The participants agreed that "one size does not fit all" when it comes to treating patients with migraine disease and that health care providers must realize that "every person's body does what it wants to do with medications." The health care provider's role must be to find a combination of things that help and to take a personalized approach to care.

The participants also agreed that health is not just the absence of physical symptoms. Patients feel empowered when they can take control of how well they feel. Well-being is a skill to learn and a nice adjunct to treating disease.

Health care providers must also be careful to not place blame on women regarding lifestyle, not be quick to judge and should also consider a patient's adverse childhood experiences. However, lifestyle and diet are an important part of managing migraine disease and health care providers should be more educated about that so they can give current information and guidance. For example, patients may not understand what "eating well" and "good sleep hygiene" actually mean. Health care providers also need to consider options for patients with anxiety or depression along with migraine disease because these are strong co-morbidities. Furthermore, health care providers should be encouraged to report any adverse events that they notice in their patients in response to treatments. There is a need to educate health care providers about the existence of the FDA Adverse Event Reporting System (FAERS) and also reporting adverse events when appropriate.

There is a need for an interdisciplinary approach to treating migraine disease. In particular, more psychologists who are specifically trained in migraine disease and its triggers are needed along with better collaboration and communication between the patient's psychologist and doctor. One participant noted a need to address the patients' return back to their environment (e.g., with coworkers, family), which does not change when their treatment changes. Patients return to environments with the same triggers.

The participants noted the importance of focusing on the consequences of migraine disease (e.g., loss of job, child custody) and the need to treat children early before the disease progresses. They recognized that the role of diet in migraine disease and the concept of triggers can be controversial but agreed that there are some common triggers which are frequently seen although not across the board, and what may be a trigger for one person may be a "protector" for another or have no impact. More discussions with patients about sleep is needed. Identifying sleep habits can reduce the frequency of migraine attacks. It appears that almost any sleep disorder can provoke a migraine attack. Obstructive sleep apnea and insomnia are the most common. Other common sleep conditions include insufficient sleep, restless legs, and the abnormal sleep behavior of jaw clenching. Others include circadian rhythm or "body clock" disorders, narcolepsy and sleepwalking.

Recommendations

The participants offered suggestions in two main strategy areas—education/awareness and evidence/advocacy—to address the barriers that they identified.

EDUCATION AND AWARENESS

- ▶ Provide more disease state education to health care providers. For example, reach out to more to OB/GYNs with presentations and exhibits at major conferences. Also consider conferences for nurse practitioners and primary care providers, and more migraine disease education for medical students and neurology residents. Do not assume that all practitioners are able to make a correct diagnosis.
- ▶ Engage headache specialists to talk to other health care providers, the lay public, patients, insurers and others who don't already know about migraine disease.
- ▶ Partner with patient advocacy groups to share information. Consider using social media and video chats, which can reach a large number of people.
- ▶ Reach out to people in "health care deserts," such as rural areas, inner cities and those with language barriers. Include community health care clinics and ethnic minorities; they need to be part of conversation.
- ▶ Educate school nurses to support students at all levels—from elementary school through college. There is currently little to no advocacy for children with migraine disease.
- ▶ Organize a headache symposium for employers and employees to discuss headache and its impact on productivity and costs.
- ▶ Stress that the patient is not alone and encourage support groups.

EVIDENCE AND ADVOCACY

- ▶ Make recommendations based on evidence and side effect profiles to determine the best options for patient satisfaction.
- ▶ Obtain more real-world data. Work with colleagues in industry to do Phase IV studies, particularly for products considered adjunct treatment.
- ▶ Report sex-specific data in clinical trials and analyze data by sex.
- ▶ Emphasize the cost-effectiveness of behavioral health.
- ▶ Shorten the path to diagnosis.
- ▶ Recognize that physicians need up-to-date electronic medical records to capture data and analyze it in their cohorts.

- ▶ Demand that others take migraine disease seriously. Work with the medical school curriculum to include migraine disease education, particularly for neurology residencies but also for primary care physicians who are commonly the first to be consulted by patients.

The results of a recent HealthyWomen survey confirmed the need for more professional and patient education regarding nondrug treatment options as well as a need for improved communication between health care professionals and patients regarding migraine treatment efficacy and satisfaction.

Conclusions

Migraine is a debilitating neurological disease that is more common in women and can have devastating effects over a woman's lifespan. Despite recent medical breakthroughs in treatment, migraine disease remains underdiagnosed and undertreated, and current drug treatments have many limitations.

Women with migraine disease have found a number of alternative nondrug therapies that are well-tolerated and have helped them manage their symptoms. The newest therapies for migraine disease are the noninvasive neuromodulation devices. These devices can be useful when medications are ineffective or incompletely effective, poorly tolerated or another tool is needed. In some cases, they may be a substitute for medication. However, they are not on top of the minds of most prescribers. The vast majority of patients with migraine disease self-treat and muddle through. All need more hope and encouragement.

In the HealthyWomen roundtable discussion, both patients and health care providers agreed that more awareness about nondrug therapies is needed to overcome the barriers to their use. Better education is needed not only for patients, but for health care providers, medical students, residents, insurance companies, and employers as well. Recommendations must be based on real-world evidence and side effect profiles. Advocacy also plays an important role in ensuring that migraine disease continues to be taken seriously.

Participants

Roundtable Participants

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About HealthyWomen

HealthyWomen is the nation's leading independent, nonprofit health information source for women. Our mission is to educate women to make informed health choices for themselves and their families so they can live and age well.

HealthyWomen connects women to health and wellness resources on our award-winning media platforms. Women trust HealthyWomen because of our 30+ year history of providing objective, research-based and accurate content. With a monthly audience of about one million, we deliver information to women in formats—from newsletters to blogs and social media channels—to fit their needs and interests. Our audience also includes health care providers, the media, policy makers and our many partners who share our commitment to women's health.

We also hear from women through our surveys and features, such as **WomenTALK®** and *Real Women, Real Stories*, which invite feedback about the health issues that concern them most and the obstacles they encounter in today's increasingly complex health care system.

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